

In the Claims

1.-2 (Currently cancelled)

3. (Cancelled)

4. - 8. (Cancelled)

9. (Currently cancelled)

10. - 11. (Cancelled)

12. (Currently amended) A purified mutant calcium-binding protein comprising an amino acid sequence as set forth in SEQ ID NO: 2 and having a substitution ~~of at least one amino acid residue in at least one calcium-binding EF hand of SEQ ID NO: 2, and wherein the calcium-binding EF hands include amino acid residues at positions 116 to 128 and 161 to 173 of SEQ ID NO: 2~~ at residue 127 or 172 of SEQ ID NO: 2.

13. - 22. (Cancelled)

23. (Currently amended) An *in vitro* method of reducing apoptosis in neuronal cells relative to apoptosis caused by presenilin 2 comprising:
administering to the neuronal cells a mutated calcium-binding protein, wherein the mutated calcium-binding protein comprises at least one substitution in the amino acid residues in the calcium-binding EF-hands of SEQ ID NO: 2, and wherein the calcium-binding EF-hands include amino acid residues at positions 116 to 128 and 161 to 173 of SEQ ID NO: 2 and wherein the substitution is at residue 127.

24. (Currently amended) An *in vitro* method to reduce induced apoptosis relative to apoptosis caused by presenilin 2, the method comprising:
administering an effective amount of the mutant calcium-binding protein comprising the amino acid sequence as set forth in SEQ ID NO: 2, wherein the mutant calcium-binding protein comprises a substitution at least one mutation selected from the group consisting of:

- ~~1) substituting at least one amino acid residue in the calcium-binding EF-hands of SEQ ID NO: 2, wherein the calcium-binding hands include amino acid residues at positions 116 to 128 or 161 to 173 of SEQ ID NO: 2; and~~
~~2) substituting at least one amino acid residue at position 2, 127 or 172 of SEQ ID NO: 2.~~

25. (Currently amended) An *in vitro* method to reduce induced apoptosis relative to apoptosis caused by presenilin 2 alone, the method comprising:

contacting cells with an effective amount of the mutant calcium-binding protein comprising an amino acid sequence as set forth in SEQ ID NO: 1 with the mutated calcium-binding protein, comprising a substitution of at least one amino acid residue in the calcium-binding EF-hands of SEQ ID NO: 2, and wherein the calcium-binding hands includes amino acid residues at positions 116 to 128 and 161 to 173 of SEQ ID NO: 2, and wherein the substitution is at residue 127 or 172.

26. (Cancelled)

27. (Currently amended) The purified mutant calcium-binding protein according to claim 12, ~~wherein the substitution of at least one amino acid residue in at least one calcium-binding EF hand of SEQ ID NO: 2 comprises amino acid residues at positions 116 to 128~~, wherein the mutation comprises replacement of an acidic residue with its amine counterpart.

28. (Currently amended) The purified mutant calcium-binding protein according to claim 27, wherein the substitution of ~~at least one amino acid residue in at least one calcium-binding EF hand of SEQ ID NO: 2 comprises~~ amino acid residue at position 127.

29. (Currently amended) The purified mutant calcium-binding protein according to claim 28, further comprising α -substitutions at amino acid residues 2 and 172.

30. - 32. (Cancelled)

33. (Currently amended) A purified mutant calcium-binding protein comprising an amino acid sequence as set forth in SEQ ID NO: 2 and having a substitution of at least one amino acid residue in at least

one calcium-binding EF-hand of SEQ ID NO: 2, and wherein the mutation comprises replacement of an acidic residue with its amine counterpart, and wherein the replacement is at residue 172.

34. (Currently amended) An *in vitro* method to reduce induced apoptosis relative to apoptosis caused by presenilin 2, the method comprising:

contacting cells with an effective amount of the mutant calcium-binding protein comprising an amino acid sequence as set forth in SEQ ID NO: 1 with the mutated calcium-binding protein, wherein the mutated calcium-binding protein comprises a substitution of at least one amino acid residue in the calcium-binding EF-hands of SEQ ID NO: 2, and wherein the substitution comprises replacement of an acidic residue with its amine counterpart at residue 127.

35. (Currently amended) A purified mutant calcium-binding protein comprising an amino acid sequence as set forth in SEQ ID NO: 2 and having a substitution of at least one amino acid residue in at least one calcium-binding EF-hand of SEQ ID NO: 2, and wherein the mutation comprises replacement of an acidic residue with its amine counterpart ~~The purified mutant calcium-binding protein according to claim 33,~~ wherein the replacement is at residue 127.